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# Zinc supplementation in the management of diarrhoea

Biological, behavioural and contextual rationale

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A continuing lack of safe water and adequate sanitation in many parts of the world means that diarrhoea remains the leading cause of death among infants and young children in low- and middle-income countries (1). Every year more than a million children under five years of age succumb to the fluid loss and dehydration associated with the majority of diarrhoea related deaths. It is estimated that 13% of all years lost due to ill-health, disability, or early death (so-called “disability-adjusted life years”) are caused by diarrhoea (2–5).

Good guidelines on the clinical management of diarrhoea among the world’s most vulnerable children therefore remain critical. There are two simple and effective treatments for the clinical management of acute diarrhoea:

- use of low concentration oral rehydration salts (ORS)
- routine use of zinc supplementation, at a dosage of 20 milligrams per day for children older than six months or 10 mg per day in those younger than six months, for 10–14 days (6, 7).

Oral rehydration is a well-known and relatively simple treatment approach (8–14). Zinc supplementation has been found to reduce the duration and severity of diarrhoeal episodes and likelihood of subsequent infections for 2–3 months (15–18). Zinc supplements are generally accepted by both children and caregivers and are effective regardless of the type of common zinc salt used (zinc sulphate, zinc acetate or zinc gluconate) (7,19).

Supplementary zinc benefits children with diarrhoea because it is a vital micronutrient essential for protein synthesis, cell growth and differentiation, immune function, and intestinal transport of water and electrolytes (20–23). Zinc is also important for normal growth and development of children both with and without diarrhoea (24–26). Zinc deficiency is associated with an increased risk of gastrointestinal infections, adverse effects on the structure and function of the gastrointestinal tract, and impaired immune function (21,27–30). Dietary deficiency of zinc is especially common in low-income countries because of a low dietary intake of zinc-rich foods (mainly foods of animal origin) or

inadequate absorption caused by its binding to dietary fibre and phytates often found in cereals, nuts and legumes (31,32).

Although the benefits of zinc supplementation in the management of diarrhoea have been established, there remain a number of barriers to the widespread implementation of this treatment strategy. Currently, zinc is not used to treat most cases of diarrhoea because the known benefits of zinc supplementation are still not widely appreciated by physicians and health-care workers in developing countries (33). There is a need to establish the optimal dosage and to investigate whether the same benefits of zinc supplementation are also applicable to children in middle- or high-income nations (31). There is also concern that high zinc intakes may compete for absorption with other micronutrients such as iron and calcium. This, in turn, can have unintended negative consequences for children's health and development (31,34–36). Studies are needed to help identify subpopulations that would benefit most in resource-limited settings and to ensure access to zinc supplementation, especially for those families whose children are most at risk of diarrhoea but may not be able to afford treatments that include zinc supplements (37). However, zinc deficiency remains difficult to diagnose because measuring serum zinc levels is not necessarily accurate for this purpose (31,38).

Currently, only a very small proportion of children in need have access to zinc supplementation (37). Guidelines on the use of zinc supplementation in the management of diarrhoea may accelerate progress towards the United Nations Millennium Development Goal 4 for reducing child mortality by two-thirds by 2015 (39).

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## References

1. Podewils LJ, Mintz ED, Nataro JP, Parashar UD. Acute, infectious diarrhea among children in developing countries. *Seminars in Pediatric Infectious Diseases*. 2004; 15(3):155–68.
2. Bryce J, Boschi-Pinto C, Shibuya K, Black RE, et al. WHO estimates of the causes of death in children. *The Lancet*. 2005; 365(9465):1147–52.
3. Checkley W, Buckley G, Gilman RH, Assis AM, Guerrant RL, Morris SS, et al. Multi-country analysis of the effects of diarrhoea on childhood stunting. *International Journal of Epidemiology*, 2008, 37(4):816–30.
4. Burton MJ, Mabey DC. The global burden of trachoma: a review. *PLoS Neglected Tropical Diseases*. 2009; 3(10):e460.
5. Mathers CD, Ezzati M, Lopez AD. Measuring the burden of neglected tropical diseases: the global burden of disease framework. *PLoS Neglected Tropical Diseases*. 2007; 1(2):e114.
6. WHO. Clinical management of acute diarrhoea. Geneva/New York: World Health Organization/UNICEF; 2004. ([http://www.who.int/maternal\\_child\\_adolescent/documents/who\\_fch\\_cah\\_04\\_7/en/](http://www.who.int/maternal_child_adolescent/documents/who_fch_cah_04_7/en/))
7. WHO. Implementing the new recommendations of the clinical management of diarrhoea. Geneva: World Health Organization; 2006. ([http://www.who.int/maternal\\_child\\_adolescent/documents/9241594217/en/](http://www.who.int/maternal_child_adolescent/documents/9241594217/en/))

8. Cash RA, Nalin DR, Rochat R, Reller LB, Haque ZA, Rahman AS. A clinical trial of oral therapy in a rural cholera-treatment center. *American Journal of Tropical Medicine and Hygiene*. 1970; 19(4):653–6.

9. Mahalanabis D, Oral fluid therapy of cholera among Bangladesh refugees. *Oral fluid therapy of cholera among Bangladesh refugees*. *Johns Hopkins Medical Journal*. 1973; 132(4):197–205.

10. Mahalanabis D, Wallace CK, Kallen RJ, Mondal A, Pierce NF. Water and electrolyte losses due to cholera in infants and small children: a recovery balance study. *Pediatrics*. 1970; 45(3):374–85.

11. Nalin DR, Cash RA. Oral or nasogastric maintenance therapy in pediatric cholera patients. *Journal of Pediatrics*. 1971; 78(2):355–8.

12. Nalin DR, Cash RA, Islam R, Molla M, Phillips RA. Oral maintenance therapy for cholera in adults. *The Lancet*. 1968; 2(7564):370–3.

13. Pierce NF, Banwell JG, Rupak DM, Mitra RC, Caranasos GJ, Keimowitz RI, et al. Effect of intragastric glucose-electrolyte infusion upon water and electrolyte balance in Asiatic cholera. *Gastroenterology*. 1968; 55(3):333–43.

14. Pierce NF, Sack RB, Mitra RC, Banwell JG, Brigham KL, Fedson DS, Mondal A. Replacement of water and electrolyte losses in cholera by an oral glucose-electrolyte solution. *Annals of Internal Medicine*. 1969; 70(6):1173–81.

15. Bhutta ZA, Bird SM, Black RE, Brown KH, Gardner JM, Hidayat A, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *American Journal of Clinical Nutrition*. 2000; 72(6):1516–22.

16. WHO. Reduced osmolarity oral rehydration salts (ORS) formulation. Geneva: World Health Organization; 2001. (<http://apps.who.int/iris/handle/10665/67322>)

17. Baqui AH, Black RE, El Arifeen S, Yunus M, Chakraborty J, Ahmed S, Vaughan JP. Effect of zinc supplementation started during diarrhoea on morbidity and mortality in Bangladeshi children: community randomised trial. *BMJ*. 2002; 325(7372):1059.

18. Water with sugar and salt. *The Lancet*, 1978, 2(8084):300–1.

19. Awasthi S. Zinc supplementation in acute diarrhea is acceptable, does not interfere with oral rehydration, and reduces the use of other medications: a randomized trial in five countries. *Journal of Pediatric Gastroenterology and Nutrition*. 2006; 42(3):300–5.

20. Aggarwal R, Balachandran A, Menon U, Nagpal R, Pokharna G, Rao S, et al. Reactogenicity of a combined hepatitis A and hepatitis B vaccine in healthy Indian children and adults. *Indian Journal of Gastroenterology*. 2007; 26(5):248–9.

21. Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. *American Journal of Clinical Nutrition*. 1998; 68(Suppl. 2):447S–463S.

22. Castillo-Duran C, Heresi G, Fisberg M, Uauy R. Controlled trial of zinc supplementation during recovery from malnutrition: effects on growth and immune function. *American Journal of Clinical Nutrition*. 1987; 45(3):602–8.
23. Patel AB, Dhande LA, Rawat MS. Therapeutic evaluation of zinc and copper supplementation in acute diarrhea in children: double blind randomized trial. *Indian Pediatrics*. 2005; 42(5):433–42.
24. Bhatnagar S, Natchu UC. Zinc in child health and disease. *Indian Journal of Pediatrics*. 2004; 71(11):991–5.
25. Fischer Walker CL, Ezzati M, Black RE. Global and regional child mortality and burden of disease attributable to zinc deficiency. *European Journal of Clinical Nutrition*. 2009; 63(5):591–7.
26. Black RE, Sazawal S. Zinc and childhood infectious disease morbidity and mortality. *British Journal of Nutrition*. 2001; 85(Suppl. 2):S125–9.
27. Lukacik M, Thomas RL, Aranda JV. A meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhea. *Pediatrics*. 2008; 121(2):326–36.
28. Gebhard RL, Karouani R, Prigge WF, McClain CJ. The effect of severe zinc deficiency on activity of intestinal disaccharidases and 3-hydroxy-3-methylglutaryl coenzyme A reductase in the rat. *Journal of Nutrition*. 1983; 113(4):855–9.
29. Bhan MK, Bhandari N. The role of zinc and vitamin A in persistent diarrhea among infants and young children. *Journal of Pediatric Gastroenterology and Nutrition*. 1998; 26(4):446–53.
30. Prasad AS. Discovery of human zinc deficiency and studies in an experimental human model. *American Journal of Clinical Nutrition*. 1991; 53(2):403–12.
31. Aggarwal R, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: a meta-analysis. *Pediatrics*. 2007; 119(6):1120–30.
32. Haider BA, Bhutta ZA. The effect of therapeutic zinc supplementation among young children with selected infections: a review of the evidence. *Food and Nutrition Bulletin*. 2009; 30(Suppl. 1):S41–59.
33. Santosham M, Chandran A, Fitzwater S, Fischer-Walker C, Baqui AH, Black R. Progress and barriers for the control of diarrhoeal disease. *The Lancet*. 2010; 376(9734):63–7.
34. Abrams SA, Atkinson SA. Calcium, magnesium, phosphorus and vitamin D fortification of complementary foods. *Journal of Nutrition*. 2003; 133(9):2994S-9S.
35. Fischer Walker C, Kordas K, Stoltzfus RJ, Black RE. Interactive effects of iron and zinc on biochemical and functional outcomes in supplementation trials. *American Journal of Clinical Nutrition*. 2005; 82(1):5–12.

36. Lutter CK, Dewey KG. Proposed nutrient composition for fortified complementary foods. *Journal of Nutrition*. 2003; 133(9):3011S–20S.

37. Fischer Walker CL, Fontaine O, Young MW, Black RE. Zinc and low osmolarity oral rehydration salts for diarrhoea: a renewed call to action. *Bulletin of the World Health Organization*. 2009; 87(10):780–6.

38. Winch PJ, Gilroy KE, Doumbia S, Patterson AE, Daou Z, Diawara A, et al. Operational issues and trends associated with the pilot introduction of zinc for childhood diarrhoea in Bougouni district, Mali. *Journal of Health: Population and Nutrition*. 2008; 26(2):151–62.

39. Millenium Development Goals. United Nations (<http://www.un.org/millenniumgoals/>, accessed March 2011).

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### Declarations of interests

Conflict of interest statements were collected from all named authors and no conflicts were identified.

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### Corresponding intervention

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